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What criterion are used to establish an adequate response to immunization in the workup of a patient with immunodeficiency

8/3/2010

Q. **These are some questions about clarification on the assesment of functional antibodies in the work-up of immunodeficiency, such as with pre- and post-pneumoccoal vaccination for example.**

The guidelines for immundoeficiency 2005 on page S21 state: "... Postvaccination levels may be determined after 3 to 4 weeks. General standards of normal responses are at least a 4 fold increase for protein antigens and a 2-fold for polysaccharide antigens..."

But on page S29 they state: ".. Adequate responses to individual pneumoccocal serotypes are defined as a postimmunization antibody concentration of 1.3ug/ml, or higher or at least 4-fold over baseline..."

So is 2 fold or 4 fold increase the criteria for polysaccharide response? There seems to be a discrepancy in the guidelines.

What about 4x increase versus 1.3 ug response?

I assume a 50% increase from age 2-5 and 70% response over age 5 is still agreed on?

What about the relevance of checking hemophiilus B vacciantion response since likely it was a conjuagted vaccine given to a child and reflects only a proteiin response?

One university immunologist in our state told me he doesn't even check diptheria and tetanus titers because of possibility of variable response to vaccination to these vaccines and because polysaccharide resposnes are the most relevant. Is this correct?

Therefore, do we only need to check titers to and vaccinate and check the response to the 23 serotype uncongugated pneumoccus vaccine, and not bother checking or vaccinating with tetanus, diptheria and hemophilus for above stated reasons for the humoral part of the immunodeficiency workup?

Labcorp on their test results for 23 serotype pneumoccous state that 1.0ug is protective. The guidelines state 1.3 ug. Should I stick with 1.3ug?

If a pre-titer is undetectable, what post vaccine number is considered a true response?
At least 1 ug?

Reference
Practice Parameter for the diagnosis and management of primary

immunodeficiency;
Bonilla et al; Annals of All. 2005 S1-S63

A. Thank you for your recent inquiry.

I am going to forward your inquiry to Dr. Francisco Bonilla. As you know, he is an internationally known expert in immunodeficiency disorders, and is the lead author on the Practice Parameters that you mentioned.

As soon as I hear from Dr. Bonilla, I will forward his response to you.

Thank you again for your inquiry and we hope this response is helpful to you.

Sincerely,
Phil Lieberman, M.D.

Below is the response we received from Dr. Francisco Bonilla. Thank you again for your inquiry, and we hope this response is helpful to you.

Sincerely,
Phil Lieberman, M.D.

Response from Dr. Francisco Bonilla:
Dr. Lieberman,

Despite many years of study, the evidence base remains shaky, due to the complexity of the problem and evolving vaccine development. Real consensus is so distant as to be invisible, in spite of endless discussion.

The majority use the 4-fold rise criterion with respect to a single immunogen. With respect to pneumococcal antibody, some older literature suggests that 2-fold may be adequate, especially in children, but most practitioners (including myself) adhere to the 4-fold standard. There is a caveat that higher pre-immunization levels lead to a lower likelihood that a 4 fold rise will be seen, but this is somewhat moot, since those individuals will be considered protected for those types anyway. Note also that the 4-fold standard is most accurately speaking, itself not a “validated” number by some rigorous study of the outcomes of vaccination, but a historical standard based on the earliest immunoassays used to determine antibody responses. There is some evidence base for the 1.3 mcg/mL criterion of protection for individual types following polysaccharide immunization, but note that it is method dependent and is not strictly applicable to results from all laboratories (including most large clinical reference laboratories). Because of this, I currently use 1 mcg/mL as a convenient number. If someone has a very low pre-immunization level and has a 4-fold rise in titer, but the final level is still <1, then that would still be scored as a “non-response”.

For pneumococcus, most follow the rule for response to at least 50% of types for 2-5 years and at least 70% for above 5, no consensus for under 2, though many toddlers will have good responses to at least several types. No type has proven consistently superior immunogenicity across all studies.

I check HIB response (PRP antibody) under age 2 because it is clinically important to have adequate immunity and I boost if it is low. I don’t look in older people because I’m not convinced it has any additional impact on the evaluation of immunocompetence.

I don’t think it’s necessary to check BOTH diphtheria and tetanus, but I ALWAYS check

tetanus in addition to pneumococcus. TT and DT are among the most consistent immunogens. It is unusual to have poor TT response with good pneumococcal response, but I've definitely seen it several times and I believe it can have clinical significance.

Hope this helps, happy to discuss further.

Tony Bonilla, M.D.

PL:kl

Key Words: adequate immune response, response to pneumococcal vaccine, response to protein antigens, immunodeficiency, immunodeficiency evaluation

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